

REPLY:

We are grateful for the opportunity to answer questions from Yang et al.

We have analyzed each one of the critiques, and these are our comments to the numbered points below raised by the authors:

1) "It seems that the authors performed an integrative analysis of individual patients pooled from each individual study instead of a 'meta-analysis.'"

We performed a comprehensive literature search in the PubMed and Scopus data bases on blister-like aneurysms. The aim of the work, as specified at the end of the introductory paragraph, was "to perform a systematic review and meta-analysis of the various types of treatment to compare their efficacy and safety."

We have tried to do both and as described in the article, all included studies were noncomparative.

2) "If this is the case, did the authors exclude a study because it did not specify clinical presentation, method of treatment, or outcome?"

In the "Materials and Methods" section, we specified the exclusion criteria: "43 articles were excluded either because the patients did not have blister-like aneurysms or because the patients' presentations or angiographic outcomes were not described." Therefore, we have included only patients with specific data regarding the clinical onset or with enough detail to obtain such information.

3) "The exact criteria used for study inclusion were not clear; this problem increases the potential for publication bias."

In the third paragraph of "Materials and Methods," we specified the following: 1) patient presentation described by using validated scales (Hunt and Hess [HH] and Fisher), 2) treatment technique (endovascular, surgical, combined), 3) long-term neurologic outcome (a good neurologic outcome was defined as a modified Rankin Scale score of 2). When an mRS score was not available, good neurologic outcome was determined from the description of the clinical results (eg, terms such as "no morbidity" or "good recovery"). We think that this is clear enough.

4) "A previous systematic review of 331 patients showed that results from multivariate analysis were influenced by the number of cases in a single study and the journal Impact Factor."

We partially agree with this comment because some inadequate studies may hamper a good meta-analysis. Furthermore, another bias could be the definition of a blister-like aneurysm. Thus, in the article, we proposed a definition.

Our purpose was to offer a systematic review and meta-analysis of the various types of treatment of blister-like aneurysms on the basis of current literature. As we wrote in our article, further prospective studies are recommended to support our results.

5) "Second, for studies that did not provide information on HH or Fisher grade, did the authors assign their own scores as they did for modified Rankin Scale score? From our experience, assignment of these parameters on the basis of limited information reported in published articles can significantly bias the results."

We have included studies that provided information on HH

and Fisher grades, besides studies that described clinical and radiologic details that have allowed extraction of HH and Fisher grades. Studies that did not provide information (clinical and radiologic onset characteristics, HH or Fisher grades) have been excluded from the analysis.

We totally disagree with Yang et al that this can "significantly bias the results"; if the information is enough to extract the score (ie, a CT scan or a description of clinical status at admission), how this could alter the results?

6) "In addition, inclusion of both HH and Fisher grades simultaneously in the multivariate analysis may be inappropriate because they can provide similar information (ie, covariates)."

This is potentially true. However, multivariate analysis performed including the model, alternatively, HH or Fisher grades (with other variables) yielded similar results, thus confirming that both HH and Fisher grades are independent predictors of the clinical outcome in our study.

"In summary, the authors presented interesting results based on an integrative analysis of patients with blister-like aneurysms. Even though one acknowledges the inherent limitations of such analysis, the study can still benefit from better descriptions of the following: 1) inclusion criteria, 2) handling of missing data (eg, HH and Fisher grades, mRS), and 3) presentation of patients (SAH versus incidental)."

All these points were discussed above.

In conclusion, we hope that we have answered all the questions raised. We thank Yang et al for helping to clarify some important issues.

Probably this article has some limitations, and many times we have written that further prospective studies must be performed to confirm these results: "Larger and homogeneous cohorts of patients will help to elucidate the optimal treatment for patients with subarachnoid hemorrhage due to blister-like aneurysms" in the "Conclusions" paragraph.

Our article was reviewed by 2 independent reviewers and a Senior Editor from the *American Journal of Neuroradiology*, who are undisputed experts on this topic. The acceptance of the manuscript and publication in such an important journal confirmed the quality of our work.

Blood blister-like aneurysms are one my team's main fields of interest; we tried to do our best to add new elements to better understand these complex lesions.

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